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### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

F		FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).		
ternational Application No. International Filing Date		International Filing Date	;	Priority Date (day/month/year)	
(day/month/year)			(day/month/year) 7 November 2003		7 November 2002
	003/001483	Cartier (IDC) or	<u></u>	I IPC	
		ncation (IPC) of	national classification and		•
ıt. Cl. <sup>7</sup>	C12Q 1/68				
pplicant UN	ISEARCH LI	MITED et al			
<ul> <li>This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</li> <li>This REPORT consists of a total of 3 sheets, including this cover sheet.</li> <li>This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been the property of the</li></ul>					
	This report is also accompanied by ANNEXES, i.e., sneets of the description, claims and the same amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).				
	These annexes	consist of a tota	of 1 sheet(s).		
3. This r	3. This report contains indications relating to the following items:				
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п					
ııı.				and industrial applicability	
īV	TV Lack of unity of invention			· · · · · · · · · · · · · · · · · · ·	
v					
VI	Certa	Certain documents cited			
VII	Certa	ain defects in the	ects in the international application		
VIII	VIII Certain observations on the international application				
Date of submission of the demand  Date of completion of the report					
1 June 2004				14 February 2005	
Name and mailing address of the IPEA/AU				Authorized Officer	
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929			RALIA	MADHU K. JOGIA Telephone No. (02) 6283 2512	

		osis of the repor			
	Basis of the report  With regard to the elements of the international application:*				
,	the international application as originally filed.				
	X	the description,	pages 1-56, as originally filed,		
			pages, filed with the demand,		
			pages, received on with the letter of		
	X	the claims,	pages 58-68, as originally filed,		
			pages, as amended (together with any statement)	under Article 19,	
		•	pages, filed with the demand,	0.07.00.0005	
			pages 57, received on 07 02.2005 with the letter	of 07.02.2005	
	X	the drawings,	pages 1-23, as originally filed,		
			pages , filed with the demand,	·	
			pages, received on with the letter of		
		the sequence list	g part of the description:		
			pages , as originally filed		
		·	pages , filed with the demand		
			pages, received on with the letter of		
2.	With	regard to the lan	rage, all the elements marked above were available of	or furnished to this Authority in the language in	
-	which	h the internationa	application was filed, unless otherwise indicated und	er this item.	
	These	e elements were a	ailable or furnished to this Authority in the following translation furnished for the purposes of international	s ranguage which is.	
			ublication of the international application (under Rul		
		the language of and/or 55.3).	ne translation furnished for the purposes of internatio	nal preliminary examination (under Rules 55.2	
3.	With	regard to any nu	leotide and/or amino acid sequence disclosed in the tion was carried out on the basis of the sequence listi	e international application, the international ng:	
		-	nternational application in written form.		
	님		h the international application in computer readable	form.	
	H	_	uently to this Authority in written form.		
	Ħ	furnished subse	uently to this Authority in computer readable form.		
		international ap	at the subsequently furnished written sequence listing lication as filed has been furnished.		
		The statement been furnished	at the information recorded in computer readable for	m is identical to the written sequence listing has	
4.		The amendmen	s have resulted in the cancellation of:		
		the de	cription, pages		
		the cl	ms, Nos.		
		the dr	wings, sheets/fig.		
5.		This report has	peen established as if (some of) the amendments had isclosure as filed, as indicated in the Supplemental B	not been made, since they have been considered to ox (Rule 70.2(c)).**	
*	R	Canlacement sheets	hich have been furnished to the receiving Office in respons iled" and are not annexed to this report since they do not c	se to an invitation under Article 14 are referred to in this	
**			t containing such amendments must be referred to under it		

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

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Statement		
Novelty (N)	Claims 1-28	YES
• • • • • • • • • • • • • • • • • • • •	Claims	NO
Inventive step (IS)	Claims 1-28	YES
involute step (==)	Claims	NO
Industrial applicability (IA)	Claims 1-28	YES
industrial approachity (22)	Claims	NO

#### Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1 Am J Physiol Heart Circ Physiol (2001)

D2 J Biol Chem (1996)

D3 Biochem J (2002)

D4 FEBS Letters (1997)

D5 WO 2000/079274

D6 Archives of Biochem Biophys (1998)

D7 Oncogene (2000)

D8 Cancer Cell (2003); P,X

D9 Toxicology (1998)

#### Novelty (N) and Inventive Step (IS) Claims 1-28

The present invention relates to a process for identifying a compound which selectively induces the mitochondrial permeability transition (MPT) in proliferating cells.

While citations D1-D9 disclose and teach processes or methods for identifying compounds which induce MPT, none of the citations appear to teach or direct the skilled addressee to using this method in proliferating cells.

Therefore the invention is novel and inventive.

#### CLAIMS:

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- A process for Identifying a compound which selectively induces the mitochondrial 1. permeability transition (MPT) in proliferating cells, wherein said process comprises contacting a cell or cell extract with a compound, determining whether the compound binds to adenine nucleotide translocator (ANT), and determining whether the compound selectively induces the MPT in proliferating cells.
- A process for screening a plurality of compounds to identify a compound which 2. selectively induces MPT in proliferating cells, wherein said process comprises confacting a cell or a cell extract with the plurality of compounds, determining whether any of the compounds bind to ANT, and if so, separately determining for each of the plurality of compounds whether the compound selectively induces the MPT in proliferating cells.
- The process of claim 1 or 2, wherein selectivity for proliferating cells is determined by comparing the effect of compounds identified as binding to ANT on the MPT in proliferating cells with the effect on the MPT in non-proliferating or growth quiescent cells.
- The process of claim 1 or 2, wherein said determination of induction of the MPT involves measuring changes in Cytochrome C release.
- The process of claim 1 or 2, wherein said determination of induction of the MPT involves measuring changes in cellular superoxide concentration.
- A process of inducing MPT in a vertebrate, wherein the method comprises 6. administering to the vertebrate a therapeutically effective amount of at least one compound identified in accordance with the process of any one of claims 1 to 5, or a therapeutically effective amount of a pharmaceutical composition comprising at least one of said compounds together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.
- A process of inducing apoptosis in proliferating mammalian cells, comprising 7. administering to the mammal an apoptosis-inducing amount of a compound identified in accordance with the process of any one of claims 1 to 5, or a therapeutically effective amount of a pharmaceutical composition comprising at least one of the compounds together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.
- A process of inhibiting anglogenesis in a mammal, comprising administering to the 8. mammal an angiogenesis-inhibiting amount of a compound identified in accordance with the process of any one of claim 1 to 5, or a therapeutically effective amount of a pharmaceutical composition comprising at least one of said compounds together with a pharmaceutically acceptable carrier, adjuvant and/or diluent.

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